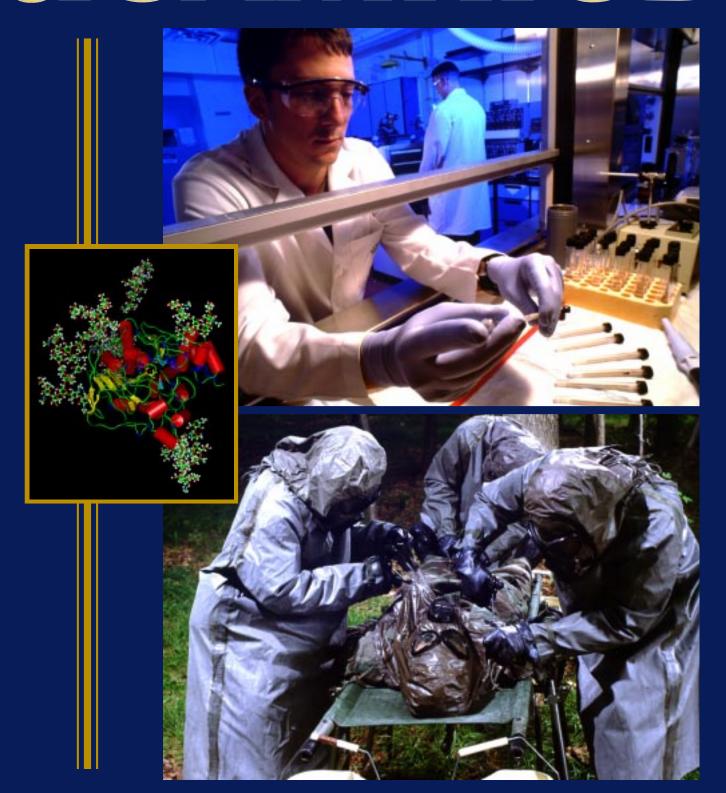
USAMRICD



U.S. ARMY MEDICAL RESEARCH INSTITUTE OF CHEMICAL DEFENSE

U.S. Army Medical Research and Materiel Command

U.S. ARMY MEDICAL RESEARCH INSTITUTE OF CHEMICAL DEFENSE

Protect, Project, Sustain

The mission of the U.S. Army Medical Research Institute of Chemical Defense (USAMRICD) is to preserve combat effectiveness by timely provision of medical countermeasures in response to Joint Service Chemical Warfare Defense Requirements. Medical chemical countermeasures protect the warfighter through antidote therapy, topical skin protectant barriers, and pretreatment protective measures, and by providing improved management of casualties through treatment regimes that reverse or reduce the toxicity of chemical agents. This mission encompasses fundamental and applied research on the pharmacology, physiology, toxicology, pathology, and biochemistry of chemical warfare (CW) agents and their medical countermeasures. The Institute also researches, as part of its mission, pharmacological countermeasures for biological warfare (BW) agents. Through its research efforts, the Institute builds a science and technology base from which it transitions new pharmaceutical, materiel, and information products for the prevention, diagnosis, treatment, resuscitation, and medical management of casualties in a CW environment. The USAMRICD also provides scientific support for the advanced development and subsequent acquisition of the products of its research, and works with Army combat developers to formulate doctrine on their use.

In addition to research, the Institute conducts a clinical training mission. The USAMRICD instructs Department of Defense (DOD) health care providers in the medical management of chemical casualties to save lives, minimize injury, maximize return to duty, and conserve fighting strength.



HISTORY



World War II era gas mask.

The USAMRICD traces its beginnings to elements of the Army Medical Department that were responsible for defense against the chemical weapons used in World War I. The earliest laboratories were first directed by the Bureau of Mines of the Department of the Interior (1917) and later by the Gas Defense Service of the U.S. Army.

In October 1922, the Medical Research Division was organized at Edgewood Arsenal. The division was formed to study the pharmacological actions of CW agents, to develop treatments for chemical casualties, and to provide information and medical recommendations to the Army about these agents. During this period, Edgewood Arsenal became the U.S. Government's center for research, development, testing, and evaluation (RDT&E) in support of chemical defense operations.

World War II brought renewed emphasis to the search for methods of preventing and treating chemical casualties. At the end of the war, the Soviets seized stocks of German-developed nerve agents and appropriated the technology for their manufacture, thus establishing the need for a strong medical chemical defense research program.

The Medical Research Division was renamed the U.S. Army Biomedical Laboratory in the early 1960s and moved into its current research and administrative building in 1968. In 1979, the laboratory added a modern comparative medicine research building.

The U.S. Army Surgeon General became responsible to the Secretary of the Army, as the Department of Defense executive agent, for all aspects of medical chemical defense in 1979. As a result, the Commanding General of the U.S. Army Medical Research and Development Command (USAMRDC) assumed responsibility for medical chemical defense RDT&E.



Chemical warfare agents were introduced on the modern battlefield during World War I.

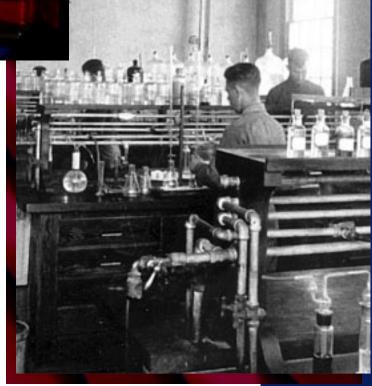


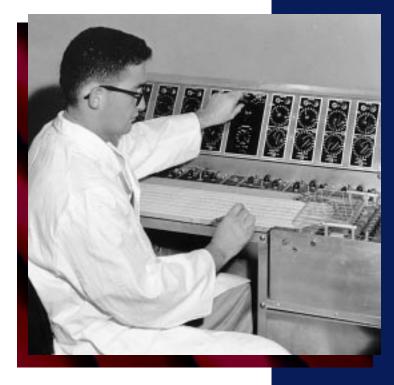
Computers and a circular dichroism spectrophotometer are used to analyze the spectra of chemical warfare agents (left). Historical photos depict an old chemistry lab during the 1950s and equipment used to gather physiological data (below).

The Biomedical Laboratory was designated the lead laboratory for medical chemical defense technology base programs by Permanent Orders 8-1, Office of The Surgeon General, Department of the Army (29 May 1979). The USAMRICD adopted its present name in 1981.

In the late 1970s and throughout the 1980s, the pace of R&D at the Institute significantly quickened in response to a renewed awareness of the threat of chemical agents and to developments in biotechnology. Significant advancements in protection and therapy for exposure to nerve agents led to a shift in emphasis in the research program to medical countermeasures for vesicating compounds, particularly sulfur mustard. In the late 1980s, program activities expanded to include basic research on neurotoxins in support of the medical biological defense research program.

Events such as the Iran-Iraq War and Operation Desert Storm have emphasized the importance of the medical chemical defense research program. Through its efforts to develop effective medical countermeasures to CW agents, the Institute's ultimate goal is to deter their use.





WORLD LEADERSHIP

The USAMRICD is a world leader in medical chemical defense research. It conducts a substantial portion of this research in-house, augmented through collaboration with several of the other laboratories and institutes of the U.S. Army Medical Research and Materiel Command (USAMRMC; formerly USAMRDC). Moreover, the USAMRICD leads the tri-service research program (Army, Navy, and Air Force) in medical chemical defense research.

Complementing the Institute's in-house efforts is an extensive extramural research program. Through this contract program, the Institute supplements its own excellent staff with experts from industry and academia, both in the United States and in other countries.



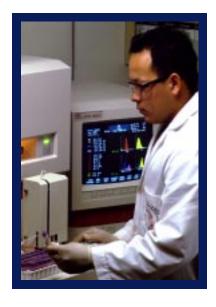
The USAMRICD also joins other countries throughout the world in information sharing and collaborative research programs that promote the advancement of scientific knowledge. The Institute's researchers participate in many national and international scientific meetings each year. The Commander, **USAMRICD** represents the United States on the North Atlantic Treaty Organization (NATO) Research Study Group 3, Panel VIII, Prophylaxis and Therapy against Chemical Agents. This vital multi-national research and development effort is crucial to the effective coordination of medical chemical defense research programs among the NATO allies.

MISSION

The USAMRICD's mission is to protect the warfighter so that a sustainable force can be projected anywhere at any time. The Institute develops pretreatments and antidotes, and provides instruction to protect and treat casualties on a chemical battlefield. While emphasis is on prevention of chemical







Investigating Agent Effects

Determining the mechanism, or mechanisms, of action of threat agents that could be encountered on a chemical/biological battlefield is a key goal of the USAMRICD. Such studies address the full spectrum of current and emerging chemical agents, as well as neurotoxins of biological origin, and are essential to development of medical countermeasures.

Medical research at the USAMRICD characterizes the pathophysiology of CW agent poisoning. For example, the effects of the highly potent nerve agents are irreversible after a time, so prompt intervention is critical. These agents can cause miosis, muscle tremors, convulsions, respiratory depression, and death.

Blister agents, or vesicants, irritate and blister the skin. They can damage the respiratory tract if inhaled, cause significant injury to the eyes, and alter the hematopoietic system at high doses.

Neurotoxins of biological origin are a diverse group of agents derived from naturally occurring organisms. They can have a variety of neurophysiological effects, including paralysis, sensory abnormalities, loss of consciousness, and convulsions.

The USAMRICD can evaluate emerging as well as documented threats. Emerging threats — an increasingly important area of research because of the lack of information on how to recognize, decontaminate, and treat exposure to these agents — present unique challenges to scientists. The USAMRICD is an unparalleled resource for identifying, tracking, and controlling medical countermeasures to new CW agents. It brings its worldwide network of researchers and 80 years of medical CW defense experience to the battle.



Developing Countermeasures

Discovering and exploring avenues of intervention to develop medical countermeasures to threat agents are key goals of the USAMRICD. These require a keen understanding not only of how specific agents affect the body, but also of how the proposed pretreatments and treatments work. Compounds or methods that show therapeutic promise must be evaluated to guarantee their safety, efficacy, and compatibility with established therapies and with other militarily relevant chemicals.



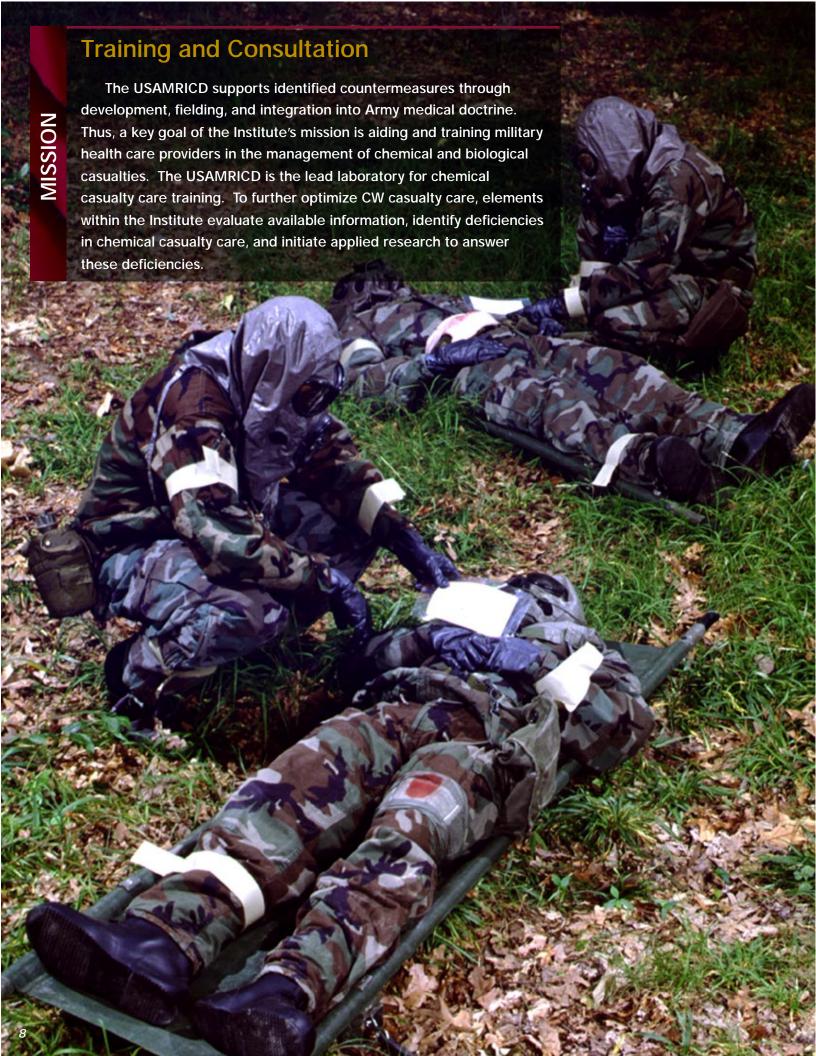
High performance liquid chromatography is used to establish the dose of novel anticonvulsants effective in preventing seizures induced by nerve chemical warfare agents.

To facilitate the search for safe and effective medical countermeasures, the USAMRICD has developed an extensive drug

screening program. Each drug
that is a candidate pretreatment,
treatment, protectant, or decontaminant is subjected to a
systematic battery of tests
designed to promote those
that are the safest and most
effective to advanced development. Included in these
tests are behavioral studies

that investigate whether these

compounds interfere with performance. Ensuring that performance on the battlefield will not be impaired is a critical factor in developing effective medical countermeasures to CW and BW agent threats.



Under the sponsorship of the Army Medical Department Center and School, and in coordination with the U.S. Army Medical Research Institute of Infectious Diseases, the USAMRICD conducts a comprehensive course of instruction in the medical management of chemical and biological agent casualties. The training educates military health care providers in the characteristics of various threat agents, the symptoms of exposure to each class of agent, and specific methods of treatment and decontamination. The course combines classroom instruction, a laboratory exercise, and field experience to establish essential skills, instill confidence, and define limitations. A weeklong course is held several times a year. Shorter versions are exported overseas and throughout the U.S. Since 1984, over 10,000 persons have received this training.

The USAMRICD also conducts a course under the sponsorship of the Office of The Surgeon General, U.S. Army on field management of chemical and biological casualties. In this course, nonmedical corps officers and noncommissioned officers involved with the acute medical management of chemical and biological casualties learn the skills necessary to provide this care in a contaminated environment. This 5-day course is offered four times a year at the USAMRICD. The course is also available in a 3-day exportable version upon request.

The USAMRICD provides consultation and guidance on the medical effects of chemical agents to the Army, Navy, Air Force, and other DOD agencies and commands.

The course's field exercise teaches the proper method of patient decontamination and familiarizes the students with equipment, such as the chemical agent monitor, and treatments, such as the Mark I Nerve Agent Antidote Kit.







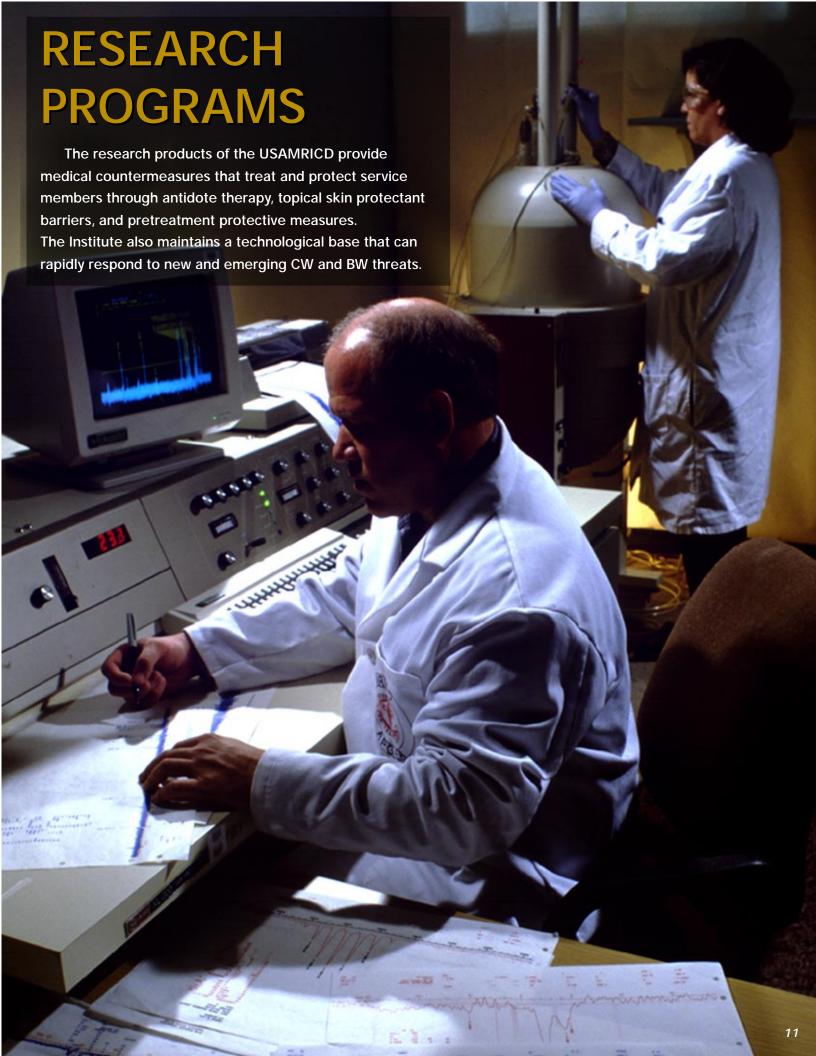


A field exercise instructor walks students through chemical agent detection with the M256A1 ticket (top). The field exercise also tests the students' ability to perform various physician tasks while wearing full protective clothing (above and right).



The Institute also provides consultation and guidance on these matters to other government authorities such as the Public Health Service and the Federal Emergency Management Agency (FEMA) when appropriate. Information used in treating battlefield exposures to CW agents is applicable to caring for mass casualties of industrial accidents and spills involving related chemicals, and is critical in caring for casualties of potential terrorist chemical weapons attacks. The USAMRICD has worked with authorities in the United States and around the world in this area. For example, the USAMRICD trained approximately 650 persons in the medical management of chemical casualties for the 1996 Atlanta Olympic Games.

The USAMRICD also participates with FEST (Foreign Emergency Support Team) for deployments outside the continental United States and with DEST (Domestic Emergency Support Team). Examples of DEST deployments include the 1996 Democratic National Convention and the 1996 Atlanta Olympic Games.



Vesicating Agents

A major portion of the Institute's effort is directed toward medical countermeasures to vesicating agents, and in particular, sulfur mustard. Sulfur mustard poses a significant threat to U.S. Armed Forces, yet its mechanisms of action have only recently begun to emerge in detail. Scientists at the USAMRICD, however, have made significant progress in defining the sequence of events following exposure



Confocal laser scanning microscopy and immunofluorescent techniques are being used to determine the effects of sulfur mustard on the cytoskeleton and adhesion complex of human epidermal keratinocytes.

to sulfur mustard, and they are examining several methods of preventing sulfur mustard-induced blister formation. Such methods include the development of scavenger molecules, intervention in the release of proteases, and control of cellular replication and metabolism. Special attention also is being given to identifying effective topical skin protectants.

Nerve Agents

Since atropine and 2-PAM chloride were fielded as the nerve agent antidote in 1983, scientists have improved their effectiveness by developing two products: pyridostigmine bromide pretreatment tablets and an anticonvulsant autoinjector containing diazepam. Research continues to examine the cause and progression of nerve agent-induced seizures to find anticonvulsants with improved efficacy against this threat.



Using computer-aided molecular modeling, the human butyrylcholinesterase enzyme has been mutated to spontaneously reactivate after its inhibition by nerve agents, thereby catalyzing the hydrolysis of nerve agents.

One of the most exciting research programs at the USAMRICD involves the pioneering efforts of its scientists to design enzyme molecules that will detoxify the nerve agent either by destroying the agent in the circulation or by physically removing the agent before it reaches its site of toxicity. These efforts employ the latest techniques in biotechnology, including enzymes tailored by site-directed mutagenesis. Scientists at the Institute have been able to show that bioscavengers can protect against nerve agent intoxication, and research efforts continue toward developing optimally mutated enzymes for this purpose.

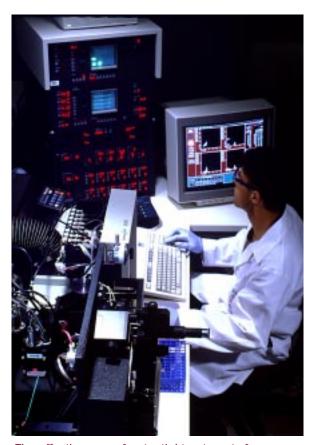
Biological Neurotoxins

The USAMRICD applies its strong neuroscience capabilities to studying the effects of biological neurotoxins on the central and peripheral nervous systems to guide development of pharmaceutical countermeasures to these threats. Of particular interest are the mechanisms of action and ion channel effects of bacterial toxins, such as botulinum toxin and toxins of marine origin. Specific studies are being carried out to investigate effects on the autonomic nervous system as well as on specific cellular and molecular processes. Building a base of understanding of these neurotoxic agents is a critical step in developing a medical defense against a variety of potentially threatening toxins. Pharmacological interventions are a particular focus of Institute efforts.



Investigators use coupled neurons of the marine mollusc Aplysia californica (right) to study the cellular effects of botulinum toxin. This animal has large, accessible nerve cells ideally suited for this research.





The effectiveness of potential treatments for chemical warfare agent toxicity is evaluated in human cell and tissue culture, using flow cytometry.

Advanced Technology

The USAMRICD has made recent groundbreaking technology base advances that have focused on medical countermeasures to the nerve and vesicant agent threats and on botulinum toxin.

A major emphasis is on development of medical countermeasures to sulfur mustard. The Institute has determined six mechanisms of action of sulfur mustard. It has developed strategies addressing those mechanisms as well as screening models with which the Institute evaluates drugs active against each mechanism to identify candidate medical countermeasures.

The advanced anticonvulsant effort is directed toward developing an anticonvulsant that is more effective and less prone to abuse than the currently fielded product.





USAMRICD scientists have determined the mechanisms

by which nerve agents induce a clinically unique seizure state, evaluated the utility of clinically approved anticonvulsants for nerve agent seizures, and identified potent centrally acting anticholinergic drugs as potential anticonvulsants.

The development of chemical agent prophylaxes or agent scavengers based on naturally occurring and artificially mutated enzymes has received considerable emphasis due to their potential as highly effective nerve agent countermeasures that require little or no additional therapy and that have few or no side effects. Proof of concept has been demonstrated in animals.

To offer an even greater level of protection than the current Topical Skin Protectant, the Institute is working on a Reactive Topical Skin Protectant, which will both protect against agent penetration to the skin and decontaminate the agent.

Consistent with its medical CW defense emphasis, the Institute is working to develop pharmaceutical countermeasures to the BW agent botulinum toxin. Scientists at the Institute have studied the molecular mechanism of botulinum toxin action and are designing and evaluating countermeasure strategies.

The Institute maintains a technological base that can rapidly respond to new and emerging CW and BW threats. Examples include the Institute's response to concerns over respiratory agents during the mid-1980s and over novel threat agents in the 1990s. USAMRICD's investigators are capable of evaluating the toxicity and mechanisms of action of emerging threats; defining the effectiveness of currently fielded medical countermeasures; and proposing and testing potential new medical countermeasures, treatment strategies, and medical management practices in response to these issues.



Chemical agent metabolites in biological fluids can be analyzed for clinical diagnosis of exposure with a liquid chromatograph interfaced to a tandem mass spectrometer.

















Knowledge gained by the Institute scientists not only helps chemical casualties, but also can further scientific inquiry into a variety of civilian medical problems. Data are published in scientific books, journals, and in government technical reports. Many of these publications are available from the Defense Technical Information Center and the National Technical Information Service.



These nerve poisons, similar to organophosphorus insecticides but much more toxic, can be fatal in unprotected troops. Survivors may suffer seizures and develop long-term brain damage. Technologies from this research program have substantially reduced the threat posed by nerve agents, and the following products have been fielded in the last decade:

- The Mark I Nerve Agent Antidote Kit consists of atropine sulfate and 2-PAM chloride in separate autoinjectors.
- ◆ Pyridostigmine bromide, a nerve agent pretreatment drug, can be administered orally to troops under risk of nerve agent attack without degrading their performance. Pyridostigmine bromide greatly increases the protection afforded by the Mark I Kit when soman or GF is the threat. It was fielded in time for use during Operation Desert Shield/Storm.
- The Convulsant Antidote for Nerve Agent consists of diazepam in an autoinjector. It is used as an adjunct therapy for nerve agent poisoning to control convulsions, protect against brain injury, and enhance survival.
- Aerosolized atropine can be administered rapidly to far-forward casualties to control respiratory symptoms.







Cyanide

Cyanide, if used as a CW agent, causes death within minutes. A pretreatment drug that will protect service members from lethal cyanide attack has recently entered advanced development.

Skin Decontamination and Protection

The M291 Skin Decontamination Kit provides the service member with a safe and effective means to decontaminate exposed skin areas. The Topical Skin Protectant, which is in advanced development, forms a barrier film on skin and augments Mission-Oriented Protective Posture gear by preventing or delaying the penetration of a wide variety of CW agents to the skin. Research is in progress on a much more effective skin barrier, the Reactive Topical Skin Protectant, that in addition to forming a skin barrier will also inactivate chemical agents.

At present, the Topical Skin Protectant is the only pharmaceutical that protects against sulfur mustard. Research directed toward development of specific treatment or pretreatment drugs against sulfur mustard is a priority for the Institute.





Chemical Casualty Management

An important part of the USAMRICD's mission is research and product development supporting clinical management of the chemical casualty, including supporting doctrine and medical materiel development. USAMRICD staff train military health care personnel in the diagnosis and treatment of chemical casualties and provide experts to support U.S. forces operating in chemical threat environments.

The Institute also publishes handbooks, technical bulletins and textbooks to guide field personnel and health care providers in the proper management and treatment of chemical agent casualties. These publications include the Field Management of Chemical Casualties Handbook; the Medical Management of Chemical Casualties Handbook; FM8-285, Treatment of Chemical Agent Casualties and Conventional Military Chemical Injuries; and TB Med 296, Assay Techniques for Detection and Exposure to Sulfur Mustard, Cholinesterase Inhibitors, Sarin, Soman, GF, and Cyanide.

Military health care providers are trained to use the M291 Personal Decontamination Kit (top) and to perform normal physician tasks in a chemical battlefield environment during the Institute's training in the medical management of chemical casualties (left).

INTERNATIONAL PROGRAMS

In light of the realities of shrinking defense budgets in the post-Cold War era, participation in international cooperative R&D is becoming increasingly important. Scientific dialogues with international counterparts, through relationships enabled by NATO and through Data Exchange Agreements, have contributed greatly to providing our service members with state-of-the-art medical defense against chemical attack. These efforts offer high payoff opportunities for leveraging U.S. investments in technology development with those of our international partners.

The foundation of international cooperation is the exchange of data and information. This takes place through collaborations and extramural contracts with internationally recognized laboratories, and visits by foreign scientists.

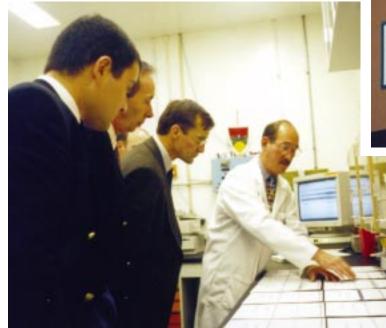
The USAMRICD collaborates with an extensive worldwide network of researchers involved in medical chemical defense research.

The Institute also coordinates biannual Medical Defense Bioscience Reviews.

These reviews of medical chemical defense research attract hundreds of scientists from all over the country and around the world.







These international research programs enable the USAMRICD to provide U.S. soldiers, sailors, airmen, and marines with the best possible medical countermeasures against chemical threat agents on the battlefield.

International cooperation is facilitated by organized forums (bilateral and multilateral) to oversee international cooperative activities. Such forums provide management oversight and direction to individual technical experts participating in international exchange programs.

In an ever-changing world environment, medical chemical defense research now, more than ever, is a multilateral effort. The ability to access current research in a manner that supports current and near-term programs is critical to the success of the USAMRICD. The benefits of international cooperation are well known and range from the highly concrete-significant savings in time and cost—to the less quantifiable—acquisition of information helpful to U.S. programs through stimulating contacts between researchers which lead to new ideas and approaches to thorny problems. These all are important to the Institute as it strives for answers to the difficult challenges posed by medical chemical defense.



The Russian Surgeon General and a delegation of Russian military physicians listen as a biochemist at the USAMRICD explains her research on the physiological effects of exposure to sulfur mustard (left).

CXIT

Visitors from Singapore get a demonstration of the USAMRICD's telemedicine capabilities (right).

ACADEMIC AND INDUSTRIAL PARTNERSHIPS



An army officer from the Republic of Korea is one of several foreign scientists to spend a year doing research at the USAMRICD.

USAMRICD has partnerships with educational institutions, large and small businesses, and nonprofit organizations...

Zambon Group
Ec&Care, Ltd.

Magainin Pharmaceuticals Inc.

The University of Georgia

Through an active technology transfer program, which includes Cooperative Research and Development Agreements (CRDAs), Materiel Transfer Agreements (MTAs), and extramural research contracts, the Institute has formed productive working relationships with universities, private industry, and research foundations. These programs facilitate the movement of technological advances made in military research laboratories to the civilian sector and the application of civilian advances to medical CW and BW defense. CRDAs and MTAs have enabled the Institute to acquire compounds and technologies still in research and development.

Recent examples of successful technology transfers include drugs and other therapies for the treatment of a variety of chemical exposure injuries; emergency medical procedures; and information on the medical evaluation and management of chemical casualties. USAMRICD's ability to leverage expertise and resources through academic and industrial partnerships greatly benefits the service member in particular and the nation in general.

Institute research managers direct millions of dollars worth of extramural research proposals a year. The Institute also administers a summer faculty program, augmenting its summer work force with trained scientists who are either college- or high-school-level faculty.

Community Outreach

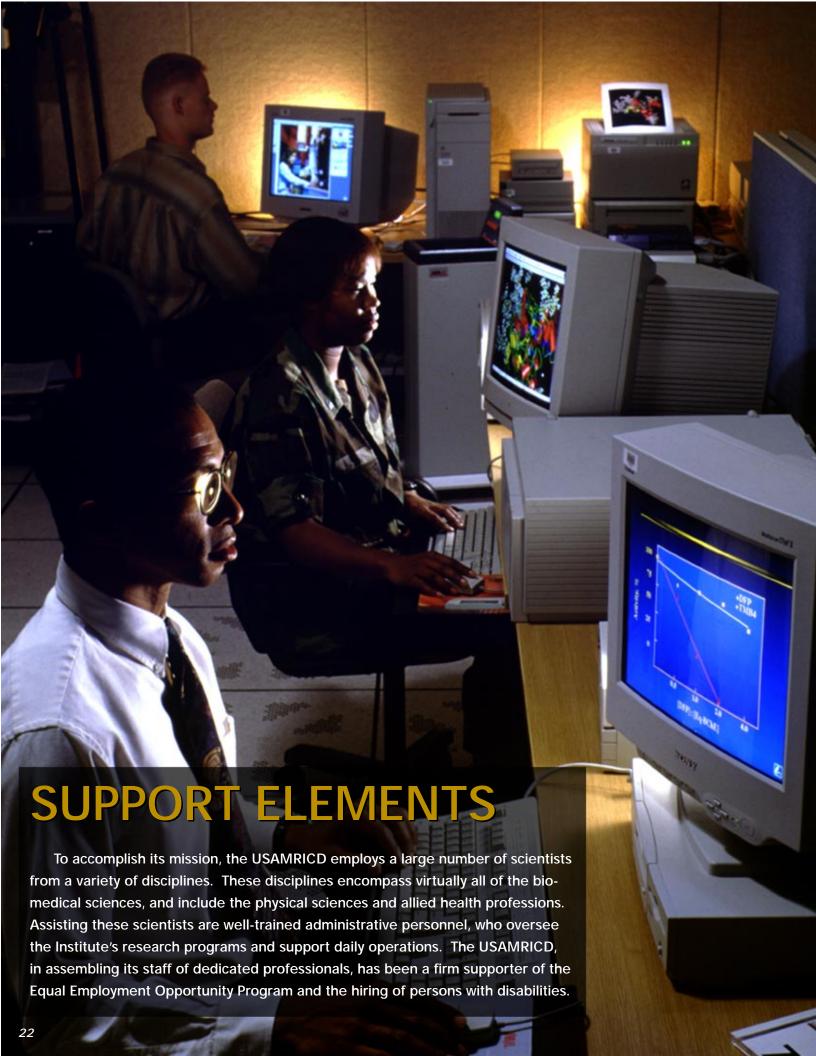
The USAMRICD invests significant effort into community outreach and involvement. The Institute has received an Aberdeen Proving Ground Community Spirit Award for a "Partners in Education" program. This program was recognized as a model for providing guidance and outreach for inexperienced, disabled students from the Harford County School System.

The Institute has received the Harford County Executive's Partnership Award as Employer of the Year, recognizing the Institute's "admirable efforts to hire people with disabilities."

In addition, the Institute received the Disability Awareness Organization of the Year Award from the Aberdeen Proving Ground Committee for the disABLED, recognizing USAMRICD's continuing efforts to provide an accommodating workplace for its disabled employees and its efforts to provide employment opportunities for students with disabilities, helping them to gain experience and self-confidence.

The USAMRICD has been named the Large Employer of the Year by the Maryland Governor's Committee on Employment of People with Disabilities. The award honors those who have distinguished themselves on behalf of others with disabilities. The USAMRICD became eligible to compete for this award after being named Public Employer of the Year by the Harford County Committee on Employment of People with Disabilities.





Research Support

An important element of support is provided by the Institute's pathologists and histologists. These scientists investigate the pathological effects associated with chemical and biological toxin injury. They examine the gross, histopathological, and ultrastructural changes observed with exposure to these agents, and evaluate the efficacy of prophylactic and therapeutic compounds in preventing or minimizing the ultrastructural injury resulting from chemical agent toxicity.

Chemists at the USAMRICD provide significant support to research efforts through methods development and consultation on prophylactic drugs and therapeutic compounds. In addition, they perform unique studies in support of the mission, such as the development of diagnostic methods that will assist a physician in the evaluation of a potential casualty.

The USAMRICD's laboratory animal veterinarians provide consultation in laboratory animal medicine and science. They play an important role in maintaining the Institute's accreditation from the Association for Assessment and Accreditation of Laboratory Animal Care International. Through a comprehensive animal care and husbandry program, they ensure that the USAMRICD meets all applicable laws, regulations, and standards concerning laboratory animal care and use, and support the Institute's commitment to minimizing use of animals in research.



Institute laboratory animal veterinarians (top) and animal caretakers (right) provide the Institute's animal colony with a quality living environment. Veterinarians provide comprehensive care that includes surgery, radiology, and pharmacology.



The Wood Technical Library maintains over 13,000 journal holdings, 7,089 book titles, and 2,000 translations to assist the technical staff.



Biomedical maintenance technicians oversee the repair of much of the Institute's sophisticated equipment.





Members of the Institute's safety staff consult with the scientific staff to ensure that proper personal protection is used in the laboratory environment.



The Wood Technical Library's on-line search capabilities give the technical staff access to hundreds of databases, including DIALOG, AGRICOLA, and the Defense Technical Information Center.



Supply personnel support the material needs of the staff through acquisition and distribution of equipment and office supplies (left). A sophisticated computer graphic capability is maintained for the creation of briefing slides and poster presentations for scientific meetings (below).



Administrative Support

Surety, safety, and environmental experts on the Institute's staff also ensure compliance with local, state, and federal regulations in their respective fields. They provide guidance and policies related to the storage, handling, use, transport, and disposal of chemical surety materiel. They conduct facility inspections and provide general occupational health guidance. They manage the Institute's Radiation Protection and Environmental Management Programs. Environmental awareness is a high priority within the Institute, and its staff has embraced local recycling programs.

Personnel in research operations and administrative support areas administer the Institute's Quality Assurance, Contracting, Technology Transfer, Public Affairs, Foreign Science Information, and International Research and Development Programs. They oversee physical security, maintenance of equipment and facilities, logistics requirements, and management of the Institute's personnel and budget.

To support its scientists' research efforts, the USAMRICD maintains its own technical library and provides a state-of-the-art information management system for Institute-wide scientific and administrative support. In addition, the USAMRICD maintains a sophisticated computer capability for the production of presentation graphics, providing material for briefings and high impact slides and posters for the scientists' professional meetings.

USAMRICD's Vision...

To be clearly recognized as the world's center of excellence for enhancing military readiness through the development of medical countermeasures for chemical agents and through training in the medical management of chemical casualties.
